METHODS FOR MEASURING IN VIVO CYTOKINE PRODUCTION

ABSTRACT

Fred D. Finkelman

Suzanne C. Morris

The present invention involves techniques for evaluating in vivo cytokine production through the in vivo capture of secreting cytokines by labeled cytokine-binding reagents, followed by in vitro measurement of serum levels of captured cytokine. The methods of the present invention make use of the ability of a neutralizing antibody to a cytokine, when injected into a person or experimental animal, to bind that cytokine and prevent its catabolism, excretion, or binding to a cytokine receptor. This causes the cytokine, which may normally have a very short in vivo half life, to accumulate in vivo as a cytokine/anti-cytokine antibody complex. If the anti-cytokine antibody is either labeled with a molecule that can be bound by another molecule (*e.g.;* biotin, which is bound by avidin or streptavidin), or is itself capable of being bound by another molecule (*e.g.;* a rat anti-cytokine antibody could be bound by an anti-rat immunoglobulin antibody), and the cytokine can also be bound by an antibody that recognizes a site distinct on the cytokine molecule from the site bound by the injected, neutralizing antibody, than the concentration of the cytokine/anti-cytokine complex in serum or other biological fluid can easily be assayed by a modified ELISA. This assay may be used with target analytes other than cytokines, which may include hormones, drugs or other analytes in a human or animal. The target analyte is preferably a macromolecule, more preferably a protein, and most preferably a cytokine.